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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/712,782	11/12/2003	Ping Jiang	312762004100	7794

25225 7590 11/30/2006

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EXAMINER	
SANG, HONG	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 11/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/712,782	JIANG ET AL.	
	Examiner	Art Unit	
	Hong Sang	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 5-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2 and 5-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RE: Jiang et al.

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/22/06 has been entered.

2. Claims 1, 2, and 5-11 are pending. Claims 3 and 4 are cancelled.

3. Claims 1, 2, and 5-11 are under examination.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Objections Withdrawn

5. The objection to claims 1, 2 and 5-11 for reciting the phrase "separate from any cells that do not produce said first fluorescent protein" in claim 1 is withdrawn in view of applicants' persuasive arguments.

6. The rejection of claims 1, 2, and 5-11 under 35 U.S.C. 112, first paragraph because of new matter is withdrawn in view of applicants' amendment to the claims to cancel the new matter.

Response to Arguments

7. The rejection of claims 1, 2 and 5-11 under 35 U.S.C. 103(a) as being unpatentable over Hadjantonakis et al. in view of Rashidi et al. (Clin. Exp. Metastasis 2000, 18: 57-60) and Trumper et al. (Blood, 1993, 81(11): 3097-3115) is maintained.

The response states that the claims are intended that the living cells are simply picked out of the tissue surgically. The response states that individual cells that produce a fluorescent protein are simply picked out of the tissue leaving behind any cells that do not produce this protein, therefore, the claims are clearly distinguished from the combination of Hadjantonakis and Trumper. While Hadjantonakis teaches manual dissection of the tissue, but the dissection does not separate the fluorescent cells from non-fluorescent cells, it is only after enzymatic dissociation and flow-cytometry that this is accomplished in a separate step. Thus, there is no mechanical separation from the tissue of cells that fluoresce from all cells that do not using surgical techniques. Moreover, while Trumper teaches mechanical separation of cells that fluoresce from those that do not, Trumper does not teach mechanically separateing the fluorescent cells from non-fluorescent cells in the surrouding tissue.

Applicants' arguments have been carefully considered but are not found persuasive. Claim 1 as currently amended comprises the active steps: mechanically separating one or more living cells that produce a fluorescent protein from any cells in the surrounding tissue that do not produce said first fluoresenct protein using surgical procedures, thereby recovering one or more living cells that produce said first flurescent protein separate from any cells that do not produce said first fluoresecnt protein. While

applicants argue that the claims are intended that the living cells are simply picked out of the tissue surgically, the claims as currently written do not limit the method to a single step (i.e. directly pick living cells out of the tissue surgically). Moreover, the transition "comprises' in a method claim indicates that the claim is open-ended and allows for additional steps (see MPEP §211.03). The combination of Hadjantonakis and Trumper teaches mechanically (surgically) removing the flurescent cells from surrounding tissue, mechanically making a cell suspention (by mincing the tissue in a buffer and pressing the minced tissue gently through a mesh, see Trumper), and surgically separating the fluorescent cells from non-fluoresent cells under microscope. Therefore, Hadjantonakis and Trumper teach every limitation of the claims.

Furthermore, Hadjantonakis teaches manual dissection of a region of interest (tissue that comprises GFP expressing cells) from a subject (see page 56, Fig.4). Because the instant claims are drawn to mechanically separating one or more living cells that produce fluorecent protein (emphasis added), Hadjantonakis teaches mechanical separation of a region comprising more than one GFP expressing cells from surrounding tissue. While Hadjantonakis does not teach mechanical separation of a single GFP expression cell from GFP non-expressing cells, Trumper teaches selecting the desired cell under inverted microscope with the help of a micromanipulator (see page 3096, last paragraph, page 8907, 1st paragraph and Figure 1). Therefore, Hadjantonakis and Trumper together teach the instant inventions.

New Gounds of Rejections

8. Claims 1, 6, 7 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Schindler (Nature Biotechnology, 1998, Aug., 16: 719-720).

Schindler teaches a laser-based ACAS system for isolating the living cells from living tissue. The method comprises attachment of the tissue sections of interest to a thermoplastic film onto which they then bind and grow. The film used for microdissection and isolation of cells is adhered to a tissue culture plate and is specially treated to absorb the laser light. As the beam circumscribe the desired cell(s), it cuts through and heats the cut edges of the thermoplastic film, which then melted and "weld" to the tissue culture plate. In this manner, individual cells/cell groups from tissue sections are isolated on "rafts" or "cookies" that remain attached to the tissue-culture plate. The surrounding "contaminating" cells are separated from the desired cell(s) by manually pealing the unwelded film containing the unselected cells from the tissue culture plate (see page 719, right column). Schindler teaches selection, isolation and analysis of living cells from tissues expressing green fluorescent protein (GFP) chimeras and subsequent analysis of function or expression cloning of isolated GFP-containing cells (see page 719, right column). Schindler teaches that the ACAS approach provides the opportunity to use single-cell isolates from living normal and tumor tissues for either functional analysis or the preparation of clonal libraries for diverse investigations in cell biology, pharmacology, drug development, etc (see page 719, right column).

9. Claims 1, 2 and 5-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hadjantonakis et al. in view of Rashidi et al. (Clin. Exp. Metastasis 2000, 18: 57-60) and Schindler (Nature Biotechnology, 1998, Aug., 16: 719-720).

The teachings of Hadjantonakis and Rashidi have been set forth before (see final office action mailed on 6/19/2006). The teachings of Schindler are set forth above. Hadjantonakis and Rashidi et al. do not teach isolating one or more GFP positive cells directly from a tissue sample. However, these deficiencies are made up for in the teachings of Schindler.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Hadjantonakis to isolate living GFP expressing metastatic tumor cells directly from tissue samples by laser microdissection as taught by Schindler instead of by flow sorting and further transplant said tumor cells to an immunocompromised animals in view of the teaching of Schindler and Rashidi. One would have been motivated to do so because Schindler teaches that the ACAS approach provides the opportunity to use single-cell isolated from living normal and tumor tissues for either functional analysis or the preparation of clonal libraries for diverse investigations in cell biology, pharmacology, and drug development, etc, moreover the ACAS approach provides single cells and contaminant-free isolation of theses cells from tissue slices (see page 270, middle paragraph), and Rashidi et al. teach that the use of GFP-transduced Lewis lung carcinoma transplanted by surgical orthotopic implantation is a very important useful model for metastasis, angiogenesis and therapeutic studies (see abstract, last sentence). One of ordinary skill in the art

would have a reasonable expectation of success to modify the method of Hadjantonakis to isolate living GFP expressing metastatic tumor cells directly from a tissue by laser microdissection instead of by flow sorting and further transplant said tumor cells to an immunocompromised animals because Schindler teaches the method of laser microdissection of single living cells from living tissue and Rashidi et al. teach how to transplant the GFP expressing tumor cells from an immunocompromised animal to another immunocompromised animals.

10. Claims 1, 2 and 5-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hadjantonakis et al. in view of Rashidi et al. (Clin. Exp. Metastasis 2000, 18: 57-60) and Bio-Rad Microscience (Press Release 0901brm02.rls, 10/15/2001).

Claims 1, 2 and 5-11, and the teachings of Hadjantonakis and Rashidi have been set forth above. Hadjantonakis and Rashidi et al. do not teach isolating one or more GFP positive cells directly from a tissue sample. However, these deficiencies are made up for in the teachings of Bio-Rad.

Bio-Rad teaches the Clonis workstation, a non-contact microdissection system for work with live cells. Using Clonis workstation, it is possible to isolate live, anchorage dependant cells from mixed cultures, and to perform secondary cutting of tissue sections (both fixed and living) placed on top of the film.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Hadjantonakis to isolate living GFP expressing metastatic tumor cells directly from tissue samples by using the Bio-

Rad Clonis workstation instead of by flow sorting and further transplant said tumor cells to an immunocompromised animals in view of the teaching of Bio-Rad and Rashidi. One would have been motivated to do so because Bio-Rad teaches that the Clonis workstation can be used to isolate living cell(s) directly from living tissue, and Clonis workstation is a non-contact microdissection system for work with live cells, therefore, provides contaminant-free isolation, and Rashidi et al. teach that the use of GFP-transduced Lewis lung carcinoma transplanted by surgical orthotopic implantation is a very important useful model for metastasis, angiogenesis and therapeutic studies (see abstract, last sentence). One of ordinary skill in the art would have a reasonable expectation of success to modify the method of Hadjantonakis to isolate living GFP expressing metastatic tumor cells directly from a tissue by using Clonis workstation instead of by flow sorting and further transplant said tumor cells to an immunocompromised animals because Clonis workstation is commercially available and have been proved to be a powerful method for isolating living cells from tissue, and Rashidi et al. teach how to transplant the GFP expressing tumor cells from an immunocompromised animal to another immunocompromised animals.

Conclusion

11. No claims are allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hong Sang whose telephone number is (571) 272 8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Hong Sang, Ph.D.
Art Unit 1643
Nov. 16, 2006

CHRISTOPHER H. YAEN
PRIMARY EXAMINER